

**NON-TECHNICAL ABSTRACT:**

"A Phase I/II Study of an Anti-tumor Vaccination Using  $\alpha(1,3)$ Galactosyltransferase Expressing Allogeneic Tumor Cells in Patients with Hormone Refractory Prostate Cancer."

Unfortunately, despite the best clinical efforts and breakthroughs in biotechnology, most patients diagnosed with advanced stage hormone-refractory prostate cancer continue to die from their disease. Reasons for this include that: 1) patients are often diagnosed at a time when their prostate cancer has already spread to other sites and 2) the cancer cells are resistant or become resistant to chemotherapy drugs and hormones used to treat the patient. Resistance to one type of chemotherapy agent often rapidly leads to resistance against many other chemotherapy drugs.

These reasons are the major causes of cancer progression that are usually discussed when considering treatment options for patients with disease that continues to grow and spread. However, another important part of the body should be considered-- the immune system. Scientists have clearly shown that prostate cancer cells produce a number of abnormal proteins or abnormal amounts of certain proteins found in normal prostate cells. Normally one would expect a patient to develop an immune response against these abnormal proteins found in their cancer and attack them much the way we would fight off an infection from a foreign bacteria or virus. However, for reasons that scientists do not fully understand, the immune system fails to respond to these abnormal proteins and does not attack the prostate cancer cells. This human clinical trial proposes a new way to make the immune system recognize the cancer and encourage it to attack the cancer cells.

Many people are familiar with the idea of transplants between people of organs like the kidneys or heart. When an organ transplant between two people is completed one of the problems that can occur is rejection of the donated organ by the recipient. This can occur because the immune system of the patient who receives the organ attacks the donated organ. If you were to attempt to transplant a pig heart to a human the rejection would be dramatically stronger than when organs are transplanted between two people. This is partly because lower animals express sugar-protein patterns on the surface of their cells that humans do not. In fact, our immune systems can quickly recognize tissues from lower mammals such as the pig or the mouse and destroys them.

In this project, we have put a mouse gene into human prostate cancer cells that produces these abnormal sugar patterns and stimulates the immune system to attack the prostate cancer. This strategy works well to kill other cancer cells in the laboratory, but it needs to be tried in prostate cancer patients to see if it will be effective and to determine if such a treatment causes any side effects. We propose to test this new treatment in patients with prostate cancer who are hormone refractory and that may have failed one type of chemotherapy treatment to see if it can stop, slow or destroy tumors in these patients. Patients will be injected with an anti-tumor vaccine consisting of a mixture of two types of dead human prostate cancer cells that have been genetically altered to express the mouse gene responsible for making this abnormal sugar-protein on the cells. This trial is scientifically designed and conducted in an ethical manner.